Synthesis, Characterization, and Structural Investigations of 1-amino-3-Substituted-1,2,3-Triazolium Salts, and a New Route to 1-substituted-1,2,3-triazoles

Greg Kaplan [a], Greg Drake [b], Kerri Tollison [a], Leslie Hall [b] and Tommy Hawkins [b]

[a] ERC, Incorporated

[b] Space and Missile Division, Propulsion Directorate,

Air Force Research Laboratory, 10 East Saturn Boulevard,

Edwards Air Force Base, CA 93524-7680, USA

Abstract: Quarternary salts based upon 3-alkyl substituted 1-amino-1,2,3-triazolium cations (alkyl = methyl, ethyl, n-propyl, 2-propenyl, and n-butyl) have been synthesized and characterized by vibrational spectra, multinuclear NMR, elemental analysis, and DSC studies. Subsequent diazotization of these salts results in the exclusive formation of 1-alkyl-1,2,3-triazoles. Single crystal x-ray studies were carried out for 1-amino-3-methyl-1,2,3-triazolium iodide, 1-amino-3-ethyl-1,2,3-triazolium bromide, 1-amino-3-n-propyl-1,2,3-triazolium bromide, and 1-amino-3-n-butyl-1,2,3-triazolium bromide as well as the starting heterocycle, 1-amino-1,2,3-triazole, and all of the structures are discussed.

Introduction.

The chemistry of N-substituted-1,2,3-triazoles has been well developed due to its high biological activity, however, the preparation of isomerically pure N-substituted-1,2,3-triazoles is not trivial [1-12]. Direct alkylation of 1(H)-1,2,3-triazoles usually forms mixtures of 1- and 2-substituted 1,2,3-triazoles [8,11], which are often difficult to

Report Documentation Page

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
JAN 2004		**-**

4. TITLE AND SUBTITLE	5a. CONTRACT NUMBER
Synthesis, Characterization and Structural Investigations of 1-amino-1,2,3-triazolium salts and a new route to 1-substituted-1,2,3-triazoles	5b. GRANT NUMBER
	5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)	5d. PROJECT NUMBER
Gregory Kaplan; Greg Drake; Tommy Hawkins; Kerri Tollison; Leslie Hall	**2303**
	5e. TASK NUMBER **M2C8**
	5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)	8. PERFORMING ORGANIZATION REPORT NUMBER
Air Force Research Laboratory (AFMC),AFRL/PRSP,10 E. Saturn Blvd.,Edwards AFB,CA,93524-7680	

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)	10. SPONSOR/MONITOR'S ACRONYM(S)
	11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION/AVAILABILITY STATEMENT

Approved for public release; distribution unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

Quarternary salts based upon 3-alkyl substituted 1-amino-1,2,3-triazolium cations (alkyl = methyl, ethyl, n-propyl, 2-propenyl, and n-butyl) have been synthesized and characterized by vibrational spectra, multinuclear NMR, elemental analysis, and DSC studies. Subsequent diazotization of these salts results in the exclusive formation of 1-alkyl-1,2,3-triazoles. Single crystal x-ray studies were carried out for 1-amino-3- methyl-1,2,3-triazolium iodide, 1-amino-3-ethyl-1,2,3-triazolium bromide, 1-amino-3-npropyl-1,2,3-triazolium bromide, and 1-amino-3-n-butyl-1,2,3-triazolium bromide as well as the starting heterocycle, 1-amino-1,2,3-triazole, and all of the structures are discussed.

15. SUBJECT TERMS

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			
unclassified	**unclassified**	**unclassified**		**30**	

separate, and once formed often undergo isomerization equilibria in solution [7,10,12]. Cycloaddition reactions usually lead to 1-substituted-1,2,3-triazoles [9-14], however this synthesis route is complicated by the use of hazardous reagents, e.g. organic azides and acetylenic materials. High yields of 1-vinyl-1,2,3-triazole [15] , and 1-isopropyl-1,2,3-triazole [16] have been reported, however the use of expensive 1(H)-1,2,3-triazole is required. Previously, preparations of 1,3-di-substituted-1,2,3-triazolium salts have been reported using various alkylating agents and 1-alkyl substituted 1,2,3-triazoles [17-21], also by reactions of 1,3-diaza-2-azoniallene salts with alkynes [22,23].

In the case of synthesizing 1-substituted-1,2,4-triazole systems, the use of 4-amino-1,2,4-triazole has been demonstrated as an excellent starting material [24]. Recently, the improvement and expansion of this reaction has been carried out resulting in a large new class of ionic liquids based upon 1-R-4-amino-1,2,4-triazolium cationic salts [25]. In expanding the notion that asymmetric 5-membered heterocyclic ring cations play an important role in the formation of the ionic liquids, 1-amino-1,2,3-triazole stood out as an excellent candidate for the exploration of forming a new family of asymmetric heterocyclic cations. Except for a brief mention on the amination and subsequent nitration of 1-amino-1,2,3-triazole by Tartakovsky's group in high-nitrogen endeavors [26], little else is known on the chemistry of this unusual high nitrogen heterocycle. We were able to improve the synthesis of 1-amino-1,2,3-triazole, prepare and fully characterize a new family of 1-amino-3-alkyl-triazolium halide quarternary salts. As well, a convenient method for the preparation of isomerically pure 1-alkyl-1,2,3-triazoles from these salts, was explored and does not involve the use of expensive 1(H)1,2,3-

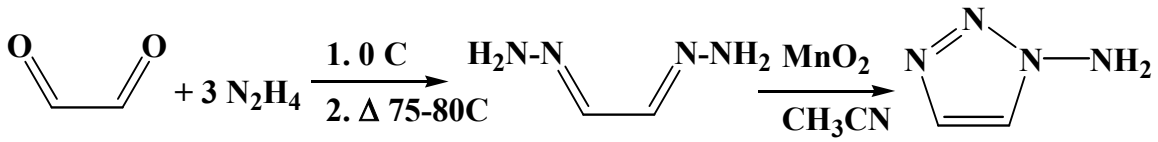
triazole. The syntheses, physical properties and spectra of all the new materials, as well as several single crystal x-ray diffraction studies will be discussed.

Results and Discussion.

Typically substituted N-amino-1,2,3-triazoles can be prepared by oxidation of corresponding substituted bishydrazone with various reagents [27,28]. However, these routes are not suitable for the oxidation of glyoxal bishydrazone (**1**) [29,30]. Previous reports and patents on the synthesis of 1-amino-1,2,3-triazole (**2**) were found to be troublesome, often difficult to repeat, with diminished yields, and often contaminated with unwanted polymeric materials [31-33].

Glyoxal bishydrazone (**1**) was prepared by modified procedure [30]. Subsequently, the hydrazone (**1**) was oxidized with manganese dioxide using acetonitrile instead of alcohol or water as the solvent (Scheme 1) unlike the previously reported synthesis [33]. This minimized oxidative coupling resulting in very high yields of 1-amino-1,2,3-triazole (**2**), which was best purified by sublimation and not crystallization.

Scheme 1

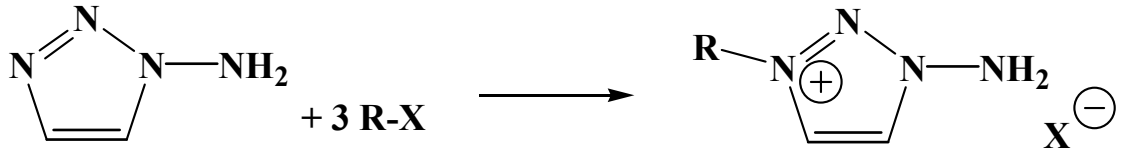


1 **2**

Alkylation reactions were carried out in polar solvents with acetonitrile being best. Reacting 1-amino-1,2,3-triazole (**2**) with an excess (>2:1) of alkyl halide insured

complete reaction as well as decreasing the overall reaction time (Scheme 2). The un-reacted alkyl halides and solvent are easily removed by vacuum distillation after reaction is complete. All of the triazolium salts (**3a-e**) were isolated as crystalline materials, were highly soluble in polar solvents such as water, methanol, ethanol, dimethylformamide, dimethylsulfoxide, acetonitrile and insoluble in chloroform, diethyl ether, and tetrahydrofuran. Unlike the weak acidic behavior noted for the 1-alkyl-4-amino-1,2,4-triazolium based salts [25], 1 M aqueous solutions of 1-amino-3-alkyl-1,2,3-triazolium halides (**3a-e**) were essentially pH neutral at 7.

Scheme 2



2 **3a**: R = CH_3, X = I

3b-3e: R = C_2H_5, C_3H_7, C_3H_5, C_4H_9, X = Br

Vibrational spectra of all the triazolium salts revealed evidence of N-alkylation of the heterocyclic ring with well defined sharp peaks in the area of 3200-3100 cm^{-1} (NH_2 stretching modes), and in the area of 3100-2900 cm^{-1} typical of both heterocyclic C-H and alkyl C-H stretching modes [34, 35] The presence of broad, intense band in the area 3300-2600 cm^{-1} is a strong evidence of complex hydrogen bonding interactions, involving N-H and C-H protons as well as $NH_2 \ldots X^-$, and are not unusual and have been observed in several other salt systems [24,25]

Proton nmr studies of the triazolium salts showed significant shifts from those observed in the starting, neutral heterocycle. Downfield shifts (average 1.0 ppm) in the heterocyclic C-H protons are observed upon alkylation of nitrogen N(3) of the 1,2,3-triazole ring, which places a formal (+1) charge on the nitrogen N(3) effectively reducing electron density in the ring from the neutral 1-amino-1,2,3-triazole (**2**). As well, a downfield shift (average shift of 1.4 ppm) of N-amino proton signal of the quarternary heterocyclic salts (**3a-e**) was observed. The proton and carbon environments of the alkyl side chains were all shifted downfield as compared to corresponding alkyl halides, most notable in the first carbon of the alkyl chains that is bonded to N(3) of the 1,2,3-triazole ring, with average downfield shifts for the protons ranging from 1.5-1.8 ppm, while for the α-carbon signal, downfield shifts ranged from 18-20 ppm in the ^{13}C spectra. These peak shifts are not unexpected and are typical for the carbon-nitrogen single bond environment [17,18,25]. Smaller downfield shifts were observed for the pendant alkyl proton environments in both the ^{1}H and ^{13}C spectra. For the heterocyclic carbon environments there were only slight shifts in the ^{13}C signals from 132 ppm to 131 ppm for C(4) and from 124 ppm to 126 ppm for C(5). These shifts can be explained from the overall formation of a cationic species, as well as the alkyl chain being bonded to the electron withdrawing triazole ring, and have been noted before in other alkylated heterocycle systems [17,18,25, 36-39].

In measuring the physical properties, it was initially thought that the quarternary salts of 1-amino-1,2,3-triazole (**2**) would have relatively low melting points, since previous studies involving 1-alkyl-4-amino-1,2,4-triazolium salts revealed significantly lower melting points than the parent 4-amino-1,2,4-triazole [25]. However, this was not

the case as 1-amino-1,2,3-triazole (**2**) melts at 49-50°C, but the quarternary salts of 1-amino-1,2,3-triazole (**3a-e**) have significantly higher melting points of 146°C (**3a**); 117-118°C (**3b**); 128-129°C (**3c**); 98-100°C (**3d**); and 131-132°C (**3e**).

Direct alkylation of 1,2,3-triazoles usually leads to mixtures of 1-alkyl- and 2-alkyl-substituted 1,2,3-triazoles [8] however, the diazotization of 1-amino-3-alkyl-1,2,3-triazolium halide salts (**3c-e**) proceeds very smoothly and produces exclusively 1-alkyl-1,2,3-triazoles (**4a-c**). These materials were recovered as volatile liquids that were distilled after work-up that were pure compounds by spectroscopic methods. The infrared spectra collected for 1-n-propyl-1,2,3-triazole (**4a**) was identical to that reported earlier [8]. The absence of N-amino NH_2 bands at 3300-3150 cm^{-1} in the vibrational as well as the disappearance of the broad N-amino group resonance in the ^1H spectra gave strong support of the formation of neutral heterocycles. As well, there were only two proton and carbon asymmetric resonances that are assignable to the two C-H 1,2,3-triazole ring environments (average upfield shift of 1 ppm ^1H; average 7 ppm upfield shift in ^{13}C spectra versus the starting heterocyclic cation carbon environments) with the easily assignable alkyl side chain resonances typical of these types of neutral heterocycles [3,4,8].

Mass spectrometry of (**4a-c**) revealed the same fragmentation pattern with molecular ions m/z 109 (**4b**), 111 (**4a**) and 125 (**4c**) being observed. All of the neutral 1-R-1,2,3-triazoles (**4a-c**) dissociated with the formation of stable fragment ions and elimination of nitrogen or alkyl groups.

Due to its high biological activity, substituted 1,2,3-triazoles have been studied extensively by single crystal x-ray diffraction. To date, all these studies focus on

substituted and annulated compounds [40-56]. However there are no reports discussing the crystal structures of any unsubstituted 1-amino-1,2,3-triazoles. We undertook x-ray crystallography studies to compare bond distances and angles in the parent 1-amino-1,2,3-triazole (**2**) to those in the quarternary salts. As expected, cation formation occurs by alkylation of nitrogen atom 3 of the 1,2,3-triazole ring. Such structures have been calculated as the energy preferred isomer by INDO//INDO calculations for aminoazoles [57].

Upon solution of all x-ray structures of quarternary 1,2,3-triazolium salts (**3a-c,e**) we found that alkylation of 1-amino-1,2,3-triazole (**2**) does not significantly affect bond distances in triazole ring, however orientation of pendant amino group appears to depend on the alkyl substitute., but most likely is a product of hydrogen bonding and chain length.

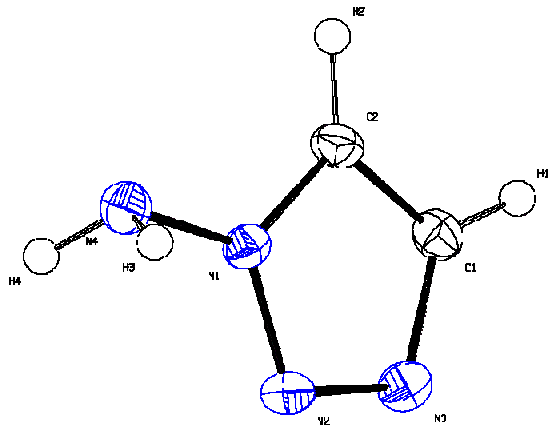


Figure 1. X-ray crystallography structure of 1-amino-1,2,3-triazole (**2**).

1-Amino-1,2,3-triazole (**2**) crystallized as a orthorhombic crystal system with $P2_12_12_1$ space group symmetry, and the crystal structure is shown in (Figure 1) and

details of the x-ray study are summarized in Table 1. Bond distances (Table 2) between N(1)-N(2) = 1.345(2) Å and N(2)-N(3) = 1.316(2) Å are in the range for partial double bonds [58], supporting delocalization of electron density, which appears in the other bond distances in the triazole ring (N(1)-C(2) = 1.343(2) Å, C(2)-C(1) = 1.359(2) Å, C(1)-N(3) = 1.363(2) Å). Protons of the amino group (N(4)-H(3) = 0.91(2) Å, N(4)-H(4) = 0.88(2) Å) saddle the plane of triazole ring above and below, pointing away from the C(2)-H(2) bond of the 1,2,3-triazole ring. This places the lone pair of the nitrogen on the amino group in the plane of the triazole ring. Strong hydrogen bonds are formed involving H(3) and H(4) protons of the amino group and the H(2) proton of the triazole ring. The most significant interaction is between the amino hydrogen H(4) and N(3)b (2.27(2) Å) compared to the hydrogen bonds H(3)…N(2)d and H(3)e…N(4) which are 2.64(2) Å and 2.66(2) Å respectively (Figure 2, Table 3).

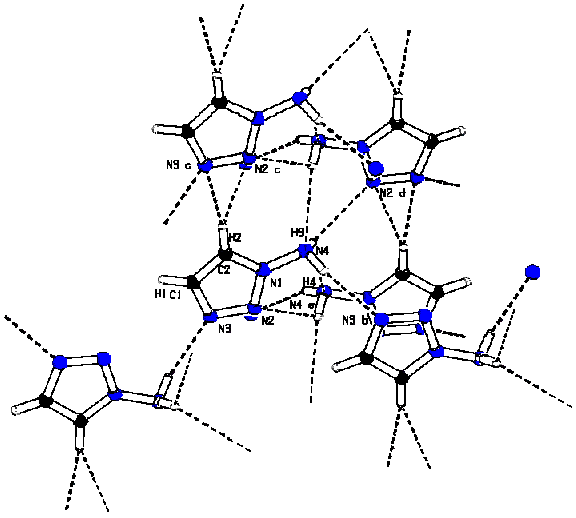


Figure 2. Significant cation-anion contacts and angles in 1-amino-1,2,3-triazole (**2**).

Table 2

Selected bonds lengths [Å] in (**2**).

N (1) – N (2)	1.345 (2)	N (4) – H (3)	0.91 (2)
N (1) – N (4)	1.398 (2)	N (4) – H (4)	0.88 (2)
N (1) – C (2)	1.343 (2)	C (1) – C (2)	1.359 (2)
N (2) – N (3)	1.316 (2)	C (1) – H (1)	0.9501
N (3) – C (1)	1.363 (2)	C (2) – H (2)	0.9502

Table 3

Significant cation-anion contact lengths [Å], angles [°] and symmetry codes in (**2**).

N (2) d…H (3) - N (4)	2.64 (2)	116 (1)	½ +x, 3/2-y, -z
N (4) e…H (3) - N (4)	2.66 (2)	131 (1)	-½+x, 3/2-y,-z
N (3) b…H (4) -N (4)	2.27 (2)	156 (2)	½-x,1-y, -½+z
N (2) c...H (2) - C (2)	2.67	159	1+x, y, z
N (3) c…H (2) - C (2)	2.52	170	1+x, y, z

1-Amino-3-methyl-1,2,3-triazolium iodide (**3a**) crystallized in a monoclinic crystal system with space group symmetry $P2_1/c$ with the asymmetric cation and anion shown in Figure 3, and details of the x-ray study are summarized in Table 1. Methylation of nitrogen atom N(3) (Figure 3) places a formal (+1) charge on N(3), slightly increases the length of the N(2)-N(3) bond (1.324(3) Å), while shortening the length of N(3)-C(1) (1.347(3) Å) as shown in Table 4. Also, there is slight increase in length of the N(1)-C(2) bond (1.351(3) Å) and a slight decrease in bond length between N(1)-N(2) (1.314(2) Å).

Overall, there are no significant changes in the C-H or N-H bond distances as compared to the neutral heterocycle (**2**).

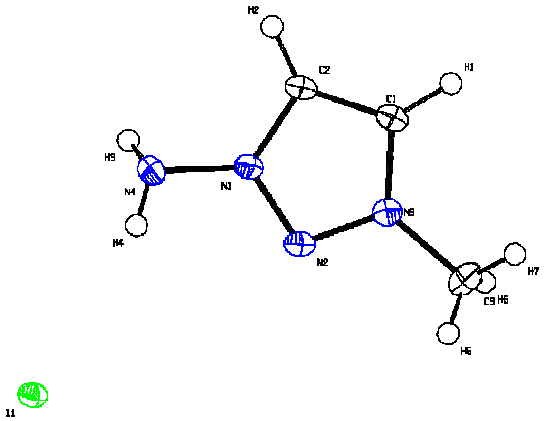


Figure 3. X-ray crystallography structure of 1-amino-3-methyl-1,2,3-triazolium Iodide (**3a**).

The increase of the N(2)-N(3) bond distance can be also attributed to the strong hydrogen bond interaction between N(3)b…H(2) = 2.67(3) Å (Figure 4, Table 5). Both protons of pendant amino group are involved in hydrogen bond interactions with the iodide anions, placing the N(4)-H(4) bond of the pendant amino group essentially in the plane of the triazole ring, and placing the lone pair out the plane of the ring. Despite these N-amino strong hydrogen bond interactions with iodide, the N-amino hydrogen bonds (N(4)-H(3) = 0.89(3) Å, N(4)-H(4) = 0.81(3) Å) are shorter than those observed in the neutral heterocycle. Both hydrogen atoms of the carbon in the 1,2,3-triazole ring (H(1)…I(1)e = 2.98(3) Å and H(2)…I(1)c = 3.15(3) Å) are involved in the hydrogen bonding interactions, slightly increasing the bond distances (C(1)-H(1) = 0.97(2) Å, C(2)-H(2) = 0.97(3) Å) from those observed in the neutral heterocycle. The protons of pendant methyl group are not involved in any hydrogen bonding interactions.

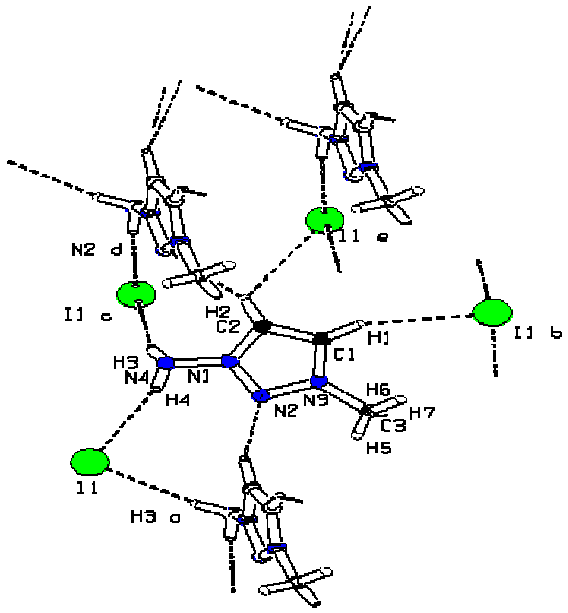


Figure 4. Significant cation-anion contacts and angles in 1-amino-3-methyl-1,2,3-triazolium iodide (**3a**).

Table 4

Selected bonds lengths [Å] in (**3a**)

N (1) – N (2)	1.314 (2)	N (4) – H (4)	0.81 (3)
N (1) – N (4)	1.386 (2)	C (1) – C (2)	1.361 (3)
N (1) – C (2)	1.351 (3)	C (1) – H (1)	0.97 (2)
N (2) – N (3)	1.324 (3)	C (2) - H (2)	0.97 (3)
N (3) – C (1)	1.347 (3)	C (3) – H (5)	0.90 (3)
N (3) – C (3)	1.461 (3)	C (3) – H (6)	0.87 (2)
N (4) – H (3)	0.89 (3)	C (3) – H (7)	0.95 (3)

Table 5

Significant cation-anion contact lengths [Å], angles [°] and symmetry codes in (**3a**).

I (1) …H (3) a - N (4)	2.74 (3)	164 (2)	x, ½-y, ½+z
I (1)…H (4) - N (4)	2.83 (3)	161 (2)	x, y, z
I (1) b…H (1) - C (1)	2.98 (3)	156 (2)	-x, -½+y, ½-z
I (1) e…H (2) - C (2)	3.15 (3)	120 (2)	-1+x, ½-y, ½+z
N (2) d…H (2) - C (2)	2.67 (3)	149 (2)	x, ½-y, ½+z

1-Amino-3-ethyl-1,2,3-triazolium bromide (**3b**) crystallized in a triclinic crystal system with P-1 space group symmetry, and the crystal structure is shown in Figure 5 and details of the x-ray study are summarized in Table 1. The protons of the N-amino group saddle the plane of the triazole ring, pointing towards the C(2)-H(2) bond, and reflect an almost 180° rotation compared to the neutral heterocycle. Protons H(3) and H(4) of the pendant amino group form strong hydrogen bonds (H(3)…Br(1) = 2.72(5) Å and H(4)…Br(1)b = 2.55(5)Å) (Figure 6, Table 7), respectively, with the corresponding bromide atoms. These hydrogen bonds might explain the rotation of the amino group. Nevertheless, the N-amino N-H bond distances are not dramatically altered. The protons attached to the carbon atoms of the 1,2,3-triazole ring (H(1)…Br(1)d = 2.85(4)Å and H(2)…Br(1)c = 2.70(4)Å) are involved in hydrogen bonding as well. The CH_2 group of the pendant ethyl is involved in weak hydrogen bonding with the bromide anion (H(6)…Br(1)e = 3.02(5)Å). However, none of the bond distances in the cation were altered significantly (Table 6).

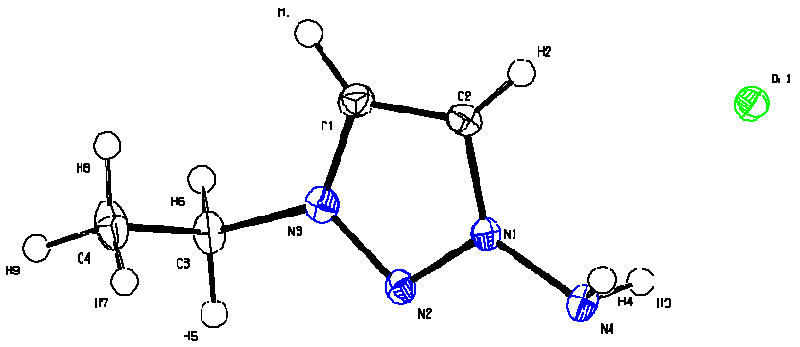


Figure 5. X-ray crystallography structure of 3-amino-1-ethyl-1,2,3-triazolium bromide (**3b**).

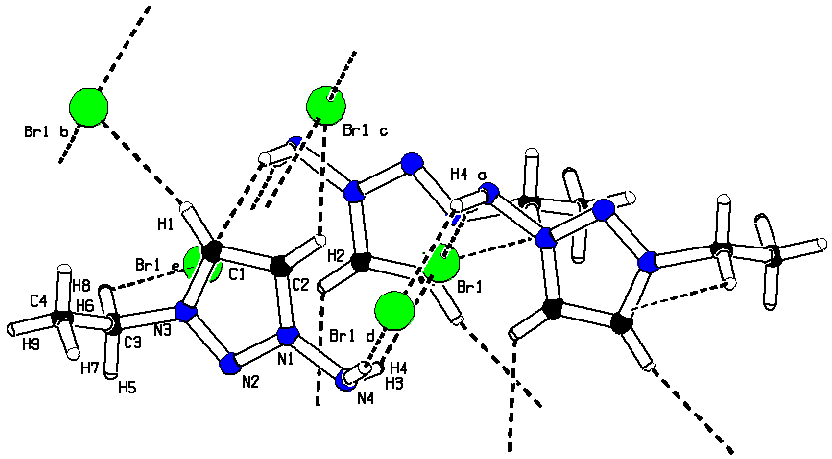


Figure 6. Significant cation-anion contacts in 1-amino-3-ethyl-1,2,3-triazolium bromide (**3b**).

Table 6

Selected bonds lengths [Å] in (**3b**).

N (1) – N (2)	1.322 (3)	C (3) – C (4)	1.507 (5)
N (1) – N (4)	1.409 (4)	C (1) – H (1)	0.94 (4)
N (1) – C (2)	1.352 (4)	C (2) – H (2)	0.95 (4)
N (2) – N (3)	1.317 (4)	C (3) – H (5)	0.99 (6)
N (3) – C (1)	1.352 (4)	C (3) – H (6)	0.94 (5)
N (3) – C (3)	1.478 (4)	C (4) – H (7)	0.94 (5)
N (4) – H (4)	0.88 (6)	C (4) – H (8)	0.96 (5)
N (4) – H (3)	0.86 (5)	C (4) – H (9)	0.97 (5)
C (1) – C (2)	1.368 (4)		

Table 7

Significant cation-anion contact lengths [Å], angles [°] and symmetry codes in (**3b**)

Br (1)…H (3) - N (4)	2.72 (5)	147 (4)	x, y z
Br (1) b…H (4) - N (4)	2.55 (5)	166 (5)	1-x,2-y,1-z
Br (1) c…H (2) - C (2)	2.85 (4)	131 (3)	1+x,y,z
Br (1) d…H (1) - C (1)	2.70 (4)	164 (3)	1-x,1-y,1-z
Br (1) e…H (6) - C (3)	3.02 (5)	124 (4)	-x,1-y,1-z

1-Amino-3-propyl-1,2,3-triazolium bromide (**3c**) crystallized in the triclinic crystal system with P-1 space group symmetry, and the crystal structure is shown in Figure 7 with details of the x-ray study summarized in Table 1. As for all the compounds

in the present study, bond distances in (**3c**) (Table 8) do not differ dramatically from the neutral heterocycle.

As described in Figure 8 and Table 9 both protons of the pendant amino group are involved in the hydrogen bonding with the bromine anions (Br(1)c…H(3) = 2.5(1) Å, Br(1)c…H(4) = 2.57(9) Å) as well as the carbon protons attached to a neighboring ring (Br(1)e…H(1) = 3.0(1) Å, Br(1)c…H(2) = 3.0(1) Å). Likewise, the H(5) and H(6) protons of the carbon of the pendant propyl group form hydrogen bonds with the corresponding bromide anions.

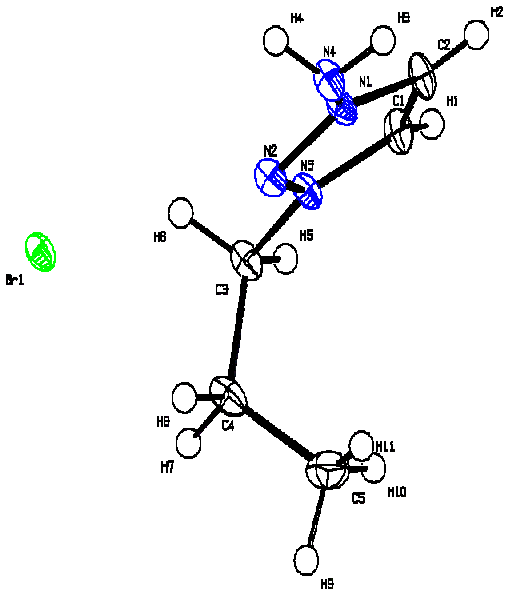


Figure 7. X-ray crystallography structure of 1-amino-3-propyl-1,2,3-triazolium bromide (**3 c**).

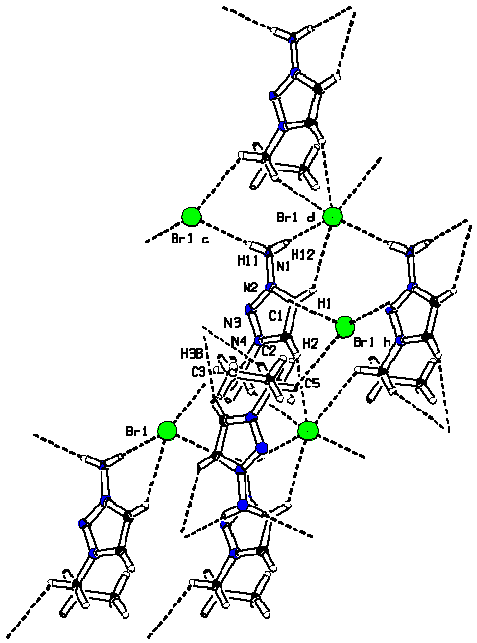


Figure 8. Significant cation-anion contacts and angles in 1-amino-3-propyl-1,2,3-triazolium bromide (**3c**).

Table 8

Selected bond lengths [Å] in (**3c**).

N (1) – N (2)	1.307 (8)	C (4) – C (5)	1.51 (1)
N (1) – N (4)	1.391 (9)	C (1) – H (1)	0.9 (1)
N (1) – C (2)	1.352 (8)	C (2) – H (2)	0.9 (1)
N (2) – N (3)	1.320 (8)	C (3) – H (5)	0.88 (8)
N (3) – C (1)	1.343 (8)	C (3) – H (6)	1.0 (1)
N (3) – C (3)	1.457 (9)	C (4) – H (7)	1.0 (1)
N (4) – H (3)	0.8 (1)	C (4) – H (8)	1.1 (1)
N (4) – H (4)	0.81 (9)	C (5) – H (9)	1.0 (1)
C (1) – C (2)	1.36 (1)	C (5) – H (10)	0.9 (1)
C (3) – C (4)	1.519 (9)	C (5) – H (11)	1.0 (1)

Table 9

Significant cation-anion contact lengths [Å], angles [°] and symmetry codes in (**3c**)

Br (1) c…H (3) - N (4)	2.6 (1)	170 (5)	1+x,-1+y,z
Br (1) d…H (4) - N (4)	2.57 (9)	176 (9)	x,-1+y,z
Br (1) e…H (1) - C (1)	3.0 (1)	144 (8)	1+x,y,z
Br (1) c…H (2) - C (2)	3.0 (1)	135 (11)	1+x,-1+y,z
Br (1) g…H (2) - C (2)	3.1 (1)	119 (10)	2-x,1-y,2-z
Br (1) e…H (5) - C (3)	3.01 (7)	163 (6)	1+x,y,z

1-Amino-3-butyl-1,2,3-triazolium bromide (**3e**) crystallized as a triclinic crystal system with P-1 space group symmetry, and the crystal structure is shown in Figure 9 with details of the x-ray study summarized in Table 1. The crystal structure of 1-amino-3-butyl-1,2,3-triazolium bromide (**3e**) reveals structure similar to 1-amino-3-propyl-1,2,3-triazolium bromide (**3c**) in distances and bond angles with no major anomalies for discussion. Both protons of the pendant N-amino group are involved in hydrogen bonding with bromine anions (Br(1)c…H(3) = 2.58(3) Å, Br(1)…H(4)b = 2.50(4) Å) as are protons attached to carbon atoms of the 1,2,3-triazole ring (Br(1)e…H(1) = 2.95(3) Å, Br(1)c…H(2) = 2.91(3) Å). The H(6) proton of the α-CH_2 of the pendant butyl group forms hydrogen bonds with the corresponding bromide anions (Figure 10, Tables 10, 11). The butyl group radiates away from the triazole ring and has assumed the low energy "zigzag" chain form as expected.

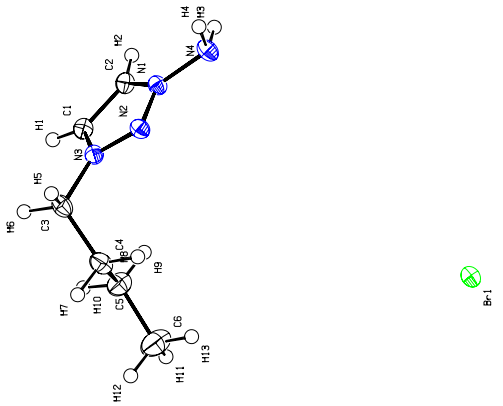


Figure 9. X-ray crystallography structure of 1-amino-3-butyl-1,2,3-triazolium bromide (**3e**).

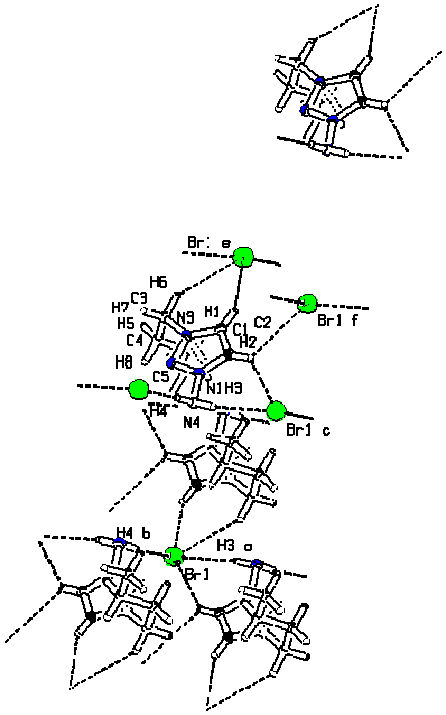


Figure 10. Significant cation-anion contacts and angles in the 1-amino-3-butyl-1,2,3-triazolium bromide (**3e**).

Table 10

Selected bonds lengths [Å] in (**3e**)

N (1) – N (2)	1.318 (2)	C (1) – H (1)	0.92 (3)
N (1) – N (4)	1.391 (2)	C (2) – H (2)	0.91 (3)
N (1) – C (2)	1.353 (3)	C (3) – H (5)	0.91 (3)
N (2) – N (3)	1.324 (2)	C (3) – H (6)	0.98 (3)
N (3) – C (1)	1.347 (3)	C (4) – H (7)	0.94 (4)
N (3) – C (3)	1.466 (3)	C (4) – H (8)	0.96 (2)
N (4) – H (3)	0.83 (3)	C (5) – H (9)	0.97 (3)
N (4) – H (4)	0.90 (4)	C (5) – H (10)	0.94 (3)
C (1) – C (2)	1.364 (4)	C (6) – H (11)	0.98 (5)
C (3) – C (4)	1.521 (3)	C (6) – H (12)	1.02 (4)
C (4) – C (5)	1.518 (4)	C (6) – H (13)	0.96 (4)
C (5) – C (6)	1.519 (4)		

Table 11

Significant cation-anion contact lengths [Å], angles [°] and symmetry codes in (**3e**).

Br (1) c…H (3) - N (4)	2.58 (3)	174 (2)	1-x,1-y,1-z
Br (1) …H (4) b - N (4)	2.50 (4)	172 (3)	2-x,1-y,1-z
Br (1) e…H (1) - C (1)	2.95 (3)	147 (3)	1-x,-y,1-z
Br (1) f…H (2) - C (2)	3.00 (2)	117 (2)	x,y,1+z
Br (1) c…H (2) - C (2)	2.91 (3)	137 (2)	1-x,1-y,1-z
Br (1) e…H (6) - C (3)	3.01 (3)	150 (2)	1-x,-y,1-z

Conclusion.

Using an improved synthesis route for 1-amino-1,2,3-triazole, a new family of 1-amino-3-alkyl-1,2,3-triazolium salts has been synthesized and characterized using mass balance, multinuclear nmr, DSC and vibrational spectroscopy. These salts have been found to be convenient starting materials in the preparation of isomerically pure 1-alkyl-1,2,3-triazoles, useful pharmaceutical intermediates. As well, several single crystal x-ray studies revealed the expected cationic structures with complex hydrogen bonding. Studies of quarternary salts of 1-amino-1,2,3-triazole are underway, investigating effects of different anions on the physical properties and structures.

EXPERIMENTAL

The starting materials, hydrazine (98%), glyoxal (40 wt % solution in water), manganese dioxide (85%), sodium nitrite (97+ %), sodium carbonate (99%), magnesium sulfate (97+%) were purchased from Aldrich Chemical Company and used without any additional purification. Methyl iodide (99.5%), ethyl bromide (98%), n-propyl bromide (99%), allyl bromide, and n-butyl bromide were purchased from Aldrich Chemical Company, Inc. and purity checked by ^{1}H and ^{13}C NMR prior to use. Methanol (99.93%, HPLC grade), ethyl acetate (99.8%, anhydrous), acetonitrile (99.93%, HPLC grade) were purchased from Aldrich Chemical Company and used without any additional purification. Diethyl ether was dried through preactivated alumina column prior to use. Infrared spectra were recorded as KBr discs (using KBr discs as a reference background) on a Nicolet 55XC FT-IR from 4000-400 cm^{-1}. Raman spectra were recorded in pyrex melting

point capillaries on Bruker Model FRA 106/S Equinox 55 Raman spectrometer equipped with a 1.06 micron IR excitation laser. NMR experiments were carried out by dissolving the salts in deuterated DMSO in 5 mm NMR tubes, and ^{1}H and ^{13}C spectra recorded on a Bruker Spectrospin DRX 400 MHz Ultrashield^{TM} NMR. Mass spectra were recorded on a GC-MS Agilent 6890A, equipped with Agilent 5973 Network mass selective detector. Thermal analyses were carried out in sealed, coated aluminum pans on a Thermal Analyst 2000, Dupont Instruments 910 Differential Scanning Calorimeter. Samples were prepared and sealed inside a nitrogen-filled glove box, and once the pans were inside the DCS cell, the cell was flushed with 10 mL per minute during heating cycles. Elemental analyses were carried out in-house on a Perkin-Elmer Series II 2400 CHNS/O elemental analysis instrument, equipped with AD6 Auto balance and by Desert Analytics, Inc of Tucson, AZ.

1-Amino-1,2,3-triazole (**2**)

In a 500 ml round bottomed flask, equipped with an over-head stirrer 14.46 g (168 mmoles) of glyoxal bishydrazone (**1**) were dispersed in 225 ml of acetonitrile at 20°C. Manganese dioxide 30.00 g (348 mmoles), was added portion-wise over a few minutes to the vigorously stirred solution. The reaction was stirred for 40 minutes whereupon additional manganese dioxide 20.00 g (232 mmoles) was added. Thin layer chromatography revealed the reaction was complete 20 minutes later and it was filtered through a plug of Celite. The filtrate was stripped down under reduced pressure leaving a viscous oil, that was sublimed yielding 12.30 g (88 %) of highly pure 1-amino-1,2,3-

triazole (**2**), mp 49-50°C; ^{1}H nmr (DMSO-d_6) : δ 7.9 (s, 1H), 7.6 (s, 1H), 6.9 (s, 2 H); ^{13}C nmr (DMSO-d_6): δ 124.0 (s), 132.3 (s).

1-Amino-3-methyl-1,2,3-triazolium iodide (**3a**)

1-Amino-1,2,3-triazole (**2**) 2.00 g (23.8 mmoles) was dissolved and stirred vigorously in 40 ml of acetonitrile at 20°C, whereupon methyl iodide 22.92 g (161.9 mmoles) was added. The reaction was stirred in darkness, being periodically monitored by thin layer chromatography until all 1-amino-1,2,3-triazole (**2**) was consumed. As the reaction progressed, white crystals of 1-amino-3-methyl-1,2,3-triazolium iodide (**3a**) precipitated. The product salt was filtered and washed with several aliquots (50 ml total) of diethyl ether. The mother liquor was concentrated by distillation under reduced pressure resulting in a second crop of crystals that were filtered, washed with diethyl ether combined with first crop and dried under high vacuum, resulting in a good yield 4.99 g (93%) of 1-amino-3-methyl-1,2,3-triazolium iodide (**3a**) , mp 146°C dec; ^{1}H nmr (DMSO-d_6) : δ 4.2 (s, 3H), 8.2 (s, 2H), 8.6 (s, 1H), 8.7 (s, 1H). ^{13}C nmr (DMSO-d_6): δ 39.7 (s), 126.8 (s), 131.5 (s).

Anal. Calcd. for $C_3H_7N_4I$: C, 15.94; H, 3.12; N, 24.79.

Found: C, 16.22; H, 3.20; N, 24.66.

1-Amino-3-ethyl-1,2,3-triazolium bromide (**3b**)

In a manner similar to that for the methyl iodide salt cited above, 1-amino-1,2,3-triazole (**2**) 2.00 g (3.8 mmoles) was reacted with ethyl bromide (12.05 g, 110.5 mmoles) at 45°C, resulting in a good yield 3.82 g (83 %) of 1-amino-3-ethyl-1,2,3-triazolium

bromide (**3b**), mp 117-118°C; DSC onset 149°C; ^{1}H nmr (DMSO-d_6): δ 1.4 (m, 3H), 4.5 (m, 2H), 8.4 (s, 2H), 8.7(s, 1H), 8.9 (s, 1H); ^{13}C nmr (DMSO-d_6): δ 14.1 (s), 48.4 (s), 126.7 (s), 130.2 (s)

Anal. Calcd. for $C_4H_9N_4Br$: C, 24.88; H, 4.70; N, 29.02.

Found: C, 24.56; H, 4.97; N, 28.90.

1-Amino-3-n-propyl-1,2,3-triazolium bromide (**3c**)

In the same manner as above 1-amino-1,2,3-triazole (**2**) 2.00 g (23.8 mmoles) was reacted with n-propyl bromide 13.60 g (110.6 mmoles) at 60°C, resulting in a good yield 4.43 gm (90%) of 1-amino-3-n-propyl-1,2,3-triazolium bromide (**3c**), mp 128-129°C; DSC onset 135°C; ^{1}H nmr (DMSO-d_6): δ 0.8 (t, 3H), 1.8 (m, 2H), 4.5 (t, 2H), 8.4 (s, 2H), 8.7 (s, 1H), 9.0 (s, 1H); ^{13}C nmr (DMSO-d_6): δ 10.3(s), 22.2(s), 54.2(s), 126.8(s), 130.5(s).

Anal. Calcd. for $C_5H_{11}N_4Br$: C, 29.00; H, 5.35; N, 27.06.

Found: C, 29.11; H, 5.32; N, 26.82.

1-Amino-3-(2-propenyl)-1,2,3-triazolium bromide (**3d**)

In the aforementioned method, 1-amino-1,2,3-triazole (**2**) 5.00 g (59.5 mmoles) was reacted with allyl bromide 35.00 g (289 mmoles) at 20°C, and upon work-up resulted in a decent yield 9.03 g (75%) of 1-amino-3-(2-propenyl)-1,2,3-triazolium bromide (**3d**), mp 100-101°C; DSC onset 135°C; ^{1}H nmr (DMSO-d_6): δ 5.2 (d, 2H), 5.4 (t, 2H), 6.0 (m, 1H), 8.4(s, 2H), 8.710 (s, 1H), 8.9(s, 1H);^{13}C nmr (DMSO-d_6): δ 54.7(s), 121.5(s), 126.8(s), 130.1(s), 130.7(s).

Anal. Calcd. for $C_5H_9N_4Br$: C, 29.29; H, 4.42; N, 27.32.

Found: C, 29.51; H, 4.42; N, 27.41.

1-Amino-3-n-butyl-1,2,3-triazolium bromide (**3e**)

Using the same method as previously mentioned, 1-amino-1,2,3-triazole (**2**) 2.00 g (23.8 mmoles) was reacted with n-butyl bromide (16.01 g., 116.8 mmoles) at 60°C. Upon work-up, 4.12 g (78%) of 1-amino-3-butyl-1,2,3-triazolium bromide (**3e**) was recovered, mp 131-132°C DCS onset 145°C; ^{1}H nmr (DMSO-d_6): δ 0.8 (m, 3H), 1.2 (m, 2H), 1.8 (m, 2H), 4.5 (m, 2H), 8.4(s, 2H), 8.7 (s, 1H), 8.9 (s, 1H); ^{13}C nmr (DMSO-d_6): δ 13.2(s), 18.7(s), 30.5(s), 52.5(s), 126.8(s), 130.6(s).

Anal. Calcd. for $C_6H_{13}N_4Br$: C, 32.59; H, 5.93; N, 25.34.

Found: C, 32.50; H, 6.21; N, 25.08.

1-n-Propyl-(1H)-1,2,3-triazole (**4a**)

1-Amino-3-n-propyl-1,2,3-triazolium bromide (**3c**) 1.56 g (7.5 mmoles) was dissolved and stirred vigorously in 10 ml of water in a 50 ml round-bottomed flask, cooled in the ice-bath. Hydrochloric acid (37%), 1.56 g (7.5 mmoles) was added slowly to the vigorously stirred triazolium solution followed by the slow, drop-wise addition of $NaNO_2$ 0.556 g (8.1 mmoles) dissolved in 1 ml of water to the acidic solution of 3-amino-1-propyl-1,2,3-triazolium bromide (**3c**). After addition was completed the reaction mixture was removed from the ice bath, stirred for 1 hour at room temperature and rendered alkaline by addition of Na_2CO_3, 4.5 g. The reaction mixture was extracted twice by 30 ml of ethyl acetate, the extracts combined, dried over magnesium sulfate, and the

ethyl acetate carefully distilled off under reduced pressure, yielding 0.72 g (87%) mmoles of 1-propyl-1,2,3-triazole (**4a**), bp 42°C (3.2×10^{-1} Torr); Mass m/e=111(M^+); ^{1}H nmr (DMSO-d_6): δ 0.8 (t, 3H), 1.8 (m, 2H), 4.3 (t, 2H), 7.7 (d, 1H), 8.1 (d, 1H); ^{13}C nmr (DMSO-d_6): δ 10.7(s), 23.2(s), 50.6(s), 124.5(s), 133.1(s).

Anal. Calcd. for $C_5H_9N_3$: C, 54.03; H, 8.16; N, 37.81.

Found: C, 53.63; H, 8.31; N, 36.74.

1-(2-Propenyl)(1H)-1,2,3-triazole (**4b**)

In the same manner as cited for the preceding 1-n-propyl-1,2,3-triazole (**4a**), 1-amino-3-(2-propenyl)-1,2,3-triazolium bromide (**3d**) 0.611 g (2.98 mmoles) was diazotized and upon workup yielded an excellent yield 0.292 g (90%). of 1-(2-allyl)-1,2,3-triazole (**4b**), bp 40°C (2.2×10^{-1} Torr); Mass m/e=109(M^+); ^{1}H nmr (DMSO-d_6): δ 5.0(m, 2H), 5.2(m, 2H), 6.0 (m, 1H), 7.7 (s, 1H), 8.0(s, 1H); ^{13}C nmr (DMSO-d_6): δ 51.4(s), 118.4(s), 124.7 (s), 132.8 (s), 133.4 (s).

Anal. Calcd. for $C_5H_7N_3$: C, 55.03; H, 6.47; N, 38.50.

Found: C, 55.41; H, 6.53; N, 38.23.

1-n-Butyl-(1H)-1,2,3-triazole (**4c**)

Using the method described above, 1-amino-3-n-butyl-1,2,3-triazolium bromide (**3e**) (1.62 g., 7.3 mmoles) was diazotized resulting in an excellent yield 0.848 g (93%) of 1-butyl-1,2,3-triazole (**4c**), bp 58°C (3.9×10^{-2} Torr) ; Mass m/e=125(M^+), 96(M- HN-N), 68(M-C_4H_9); ^{1}H nmr (d_6-dmso): δ 0.8 (m, 3H), 1.2 (m, 2H), 1.8 (m, 2H), 4.3 (m, 2H), 7.7 (s, 1H), 8.1 (s, 1H); ^{13}C nmr (d_6-dmso) δ 13.2(s), 19.0(s), 31.8 (s), 48.8 (s), 124.5(s), 133.1 (s).

Anal. Calcd. for $C_6H_{11}N_3$: C, 57.57; H, 8.86; N, 33.57.

Found: C, 57.31; H, 9.11; N, 33.49.

Acknowledgments

The authors would like to thank Michael Berman (AFOSR) and Michael Huggins (AFRL/PRS) as well as Ronald Channell (AFRL/PRSP) and Wayne Kalliomaa (AFRL/PRSP) for financial support and encouragement of this work.

REFERENCES AND NOTES

[1]. K. Thomas Finley, *Triazoles-1,2,3*, Wiley, Chapter 1., 2-6 (1980)

[2] V.V. Rostovtsev, L.G. Green, V.V. Fokin and K.B. Sharpless, *Angew. Chem. Int. Ed*., **41**, 2596 (2002)

[3]. J. Elguero, E. Gonzales and R. Jacquier, *Bull. Soc. Chim. Fr*., **8**, 2998 (1967)

[4] V.N. Kizhnyaev, F.A. Pokatilov, N.A.Tsypina, G.V. Ratovskii, L.I.Vereschagin and A.I.Smirnov, *Zh. Org. Khim.*, **38**, 1099 (2002)

[5] E. Diez-Barra, A.d.l. Hoz, A. Loupy and A. Sanchez-Migallon, *Heterocycles*, **38**, 1367 (1994)

[6]. T.L. Gilchrist, *Heterocyclic chemistry,* Longman, London, 306, 1997

[7] L.G.Tikhonova, A.V.Maksikova, E.S. Serebryakova, I.G. Kaufman and L.I. Vereshchagin, *Khim. Geterosycl. Soed*., **10**, 1417 (1982)

[8]. H.Gold, *Ann. Chem*., **688**, 205, (1965)

[9] J.A. Durden Jr., H.A. Stansburry and W.H.Catlette, *J. Chem. Eng. Data,* **9(2)**, 228 (1964)

[10] P.Ykman, G. L'abbe and G.Smets, *Tetrahedro*n, **27**, 5623 (1971).

[11] Y.Tanaka and S.Miller, *Tetrahedro*n, **29**, 3285 (1973)

[12] L.Birkhover and P.Wegner, *Chem. Ber*., **100**, 3485 (1957)

[13] R.H.Wiley, K.F.Hussung and J.Moffat, *J. Org. Chem*., **21**, 190 (1956)

[14] A. Hassner, M. Stern, H.E. Gottlieb and F.Frolow, *J. Org. Chem*., **55**, 2304 (1990)

[15] V.N. Kizhnyaev, F.A. Pokatilov, N.A.Tsypina, G.V.Ratovskii, L.I.Vereshchagin and A.I.Smirnov, *Zh. Org. Khim.*, **38**, 1056 (2002)

[16] A.O. Koren, *J.Heterocyclic Chem*., **39**, 1111, (2002).

[17]. M.Begtrup and K.V. Poulsen, *Acta Chem. Scand*., **25**, 2087 (1971)

[18]. M.Begtrup, *Acta Chem. Scand*., **25**, 3500 (1971)

[19]. M.Begtrup, *Acta Chem. Scand*., **21**, 1234 (1967)

[20] R. Mohr and H. Hertel, *Chem. Ber*., **96**, 114-129 (1963)

[21] C.S. Rondestvedt and P.K. Chang, *J. Amer. Chem. Soc*., **77**, 6540 (1955)

[22] W.Wirschun, M. Winkler, K. Lutz and J.C. Jochims, *J. Chem. Soc., Perkin Trans.*, **1**, 1755 (1998)

[23] W.Wirschun, G-M. Maier and J. C. Jochims, *Tetrahedro*n, **53**, 5755 (1997).

[24] G.D. Drake, T. Howkins, A. Brand, L. Hall, M. Mckay, A. Vij and I. Ismail, *Propellants, Explosives, Pyrotechnics,* **28**, 174 (2003).

[25] G.D.Drake et al. in press

[26] O.P.Shitov, V.A.Vyazkov and V.A.Tartakovskii, *Izv. Akad. Nauk SSSR*, *Ser. Khim*., **11**, 2654 (1989)

[27]. G.G.Bagramov, K.A.Lysenko, M.D.Bagramova and Yu.T.Struchkov, *Izv. Akad. Nauk SSSR*, *Ser. Khim*.(Russ), **44**, 2465 (1995).

[28] El Khadem and El-Shafei, *J. Org. Chem*., **41**, 3117 (1958)

[29] R.G. Gallucci, *J. Chem. Eng. Data,* **27**, 217 (1982)

[30] H.M. Fisher and R.C. Stoufer, *Inorg. Chem*., **5**, No. 7 (1966)

[31] K. Harada, M. Oda, A. Matsushita and M. Shirai, *Heterocycles*, **48**, 695 (1998)

[32] V.V. Kuz'menko, A.F. Pozharskii, *Zh. Org. Khim.*, **28**, 1320 (1992)

[33]. US patent 5,728,841 CA: P86648***b***

[34] F. Billes, H. Endredi and G. Kerestury. *Journal of Molecular Structure,* **530**, 183 (2000)

[35] E. Lieber, D. R. Levering and L.J. Patterson, *Analytical Chemistry*, **23**, 1594 (1951)

[36] G.B. Barlin, T.J. Batterham, *J. Chem, Soc.(B)*, 516, (1967)

[37] Y.R. Mirzaei, B. Twamely and J. M. Shreeve, *J. Org. Chem.,* **67**, 9340 (2002)

[38] R. P. Singh, S. Manandhar, and J. M. Shreeve, *Tetrahedron Letters*, **43**, 9497 (2002)

[39] Y.R. Mirzaei and J. M. Shreeve, *Synthesis*, 24 (2003).

[40] A.Gieren and V.Lamm, *Acta Crystallogr*., *Sect. B: Struct.Chem*., **34**, 3248 (1978)

[41] L.Parkanyi, A.Kalman, G.Argay and J.Schawarts, *Acta Crystallogr*., *Sect.B: Struct.Chem.*, **33**, 3102 (1978)

[42] S.C.Kokkou and P.J.Rentzeperis, *Acta Crystallogr*., *Sect. B: Struct.Che*m., **31**,1564 (1975)

[43] S.C.Kokkou and P.J.Rentzeperis, *Acta Crystallogr*., *Sect. B: Struct.Chem*., **31**, 2788 (1975)

[44] G.L'abbe, W.Meutermans, L.Van Meervelt, G.S.D.King and A.T.H.Lenstra, *Bull. Soc. Chim. Belg*., **97**, 179 (1988)

[45] K.Nielsen, L.Schepper and I.Sotofte, *Acta Chem. Scand*., A, **33**, 693 (1979)

[46] I.Sotofte and K.Nielsen, *Acta Chem. Scand*., A, **33**, 687 (1979)

[47] M.A.Sridhar, N.K.Lokanath, J.S.Prasad, D.G.B.Gowda and K.S.Rangappa, *Z.Kristallogr*.-*New Cryst. Struct*., **212**, 30 (1997)

[48] J.-L.M.Abboud, C.Foces-Foces, R.Notario, R.E.Trifonov, A.P.Volodenko, I.Alkorta and J.Elguero, *Eur.J.Org.Chem*., 3013 (2001)

[49] G.Boche, C.Willeke, M.Marsch and K.Harms, *Z. Kristallogr*., **211**, 583 (1996)

[50] B.Abarca, R. Ballesteros, F.Mojarrad, M.R.Metni, S.Garsia-Granda, E. Perez-Carreno and G.Jones, *Tetrahedron*, **47**, 5277 (1991)

[51] E.Laskos, P. S. Lianis, N.A.Rodios, A.Terzis and C.P.Raptopoulou, *Tetrahedron Letters*, **36**, 5637 (1995)

[52] F.Benedetti, S. Bozzini, M. Forchiassin, G. Nardin, G. Pitacco, C.Russo and E.Valentin, *J.Heterocyclic Chem*., **26**, 301, (1989)

[53] L. G. Purnell, J.C. Shepherd and D.J. Hodgson, *J. Am. Chem. Soc.*, **97**, 2376 (1975)

[54]. J.Feneau-Dupont, J.P.Declerq, E.Vanderstede and G.L'abbe, *Bull. Soc. Chim. Belg*., **98**, 415 (1989)

[55]. A.Herrero, M.L.Jimeno, C.Ochoa, J.L.G.DePaz, C. Foces-Foces, F.H.Cano and M.Martinez-Ripoll, *Heterocycles*, **34**, 1399 (1992)

[56]. C,B.Vicentini, V.Ferretti, A.C.Veronese and P.Giori, *Heterocycles*, **41**, 2409 (1995)

[57] R.M.Claramunt D. Sanz, J. Catalan, F. Fabero, N.A. Garsia, C. Foces-Foces, A.L. LIamas-Saiz and J. Elguero , *J.Chem. Soc*., *Perkin Trans*., **2**, 1687 (1993)

[58] Conquest V.1.5. Cambridge Structural Database System Version 5.24 (July Update, 2003) CCDC, Cambridge, UK (2003)